



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-D-0800]

Regulatory Classification of Pharmaceutical Co-Crystals; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a guidance for industry entitled "Regulatory Classification of Pharmaceutical Co-Crystals." This guidance provides applicants planning to submit new drug applications and abbreviated new drug applications with information on the appropriate regulatory classification of pharmaceutical co-crystal solid-state forms. It also provides information about the data that applicants should submit to support the appropriate classification of a co-crystal as well as the regulatory implications of the classification. This guidance finalizes the draft guidance for industry entitled "Regulatory Classification of Pharmaceutical Co-Crystals" published in August 2016.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2011-D-0800 for "Regulatory Classification of Pharmaceutical Co-Crystals." Received comments will be

placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff office between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the

prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document. FOR FURTHER INFORMATION CONTACT: Richard (Rik) Lostritto, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 4148, Silver Spring, MD 20993-0002, 301-796-1697.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Regulatory Classification of Pharmaceutical Co-Crystals." This guidance provides applicants planning to submit new drug applications and abbreviated new drug applications with information on the appropriate regulatory classification of pharmaceutical co-crystal solid-state forms. This guidance also provides information about the data that applicants should submit to support the appropriate classification of a co-crystal as well as the regulatory implications of the classification.

The recommendations in this guidance apply to materials that the Agency has not previously evaluated and determined to be pharmaceutical co-crystals. The recommendations do

not apply to materials that the Agency has previously designated as salts, complexes, or other non-co-crystalline forms.

Co-crystals are crystalline materials composed of two or more different molecules, typically active pharmaceutical ingredient (API) and co-crystal formers ("coformers"), in the same crystal lattice. Pharmaceutical co-crystals have provided opportunities for engineering solid-state forms beyond conventional solid-state forms of an API, such as salts and polymorphs. Co-crystals can be tailored to enhance drug product bioavailability and stability and to enhance the processability of APIs during drug product manufacture. Another advantage of co-crystals is that they generate a diverse array of solid-state forms for APIs that lack ionizable functional groups, which is a prerequisite for salt formation.

This guidance addresses the public comments received in response to the draft guidance for industry "Regulatory Classification of Pharmaceutical Co-Crystals" issued in August 2016. In response to this and other feedback from stakeholders, FDA has clarified the appropriate classification of co-crystals and addresses the concern by further clarifying that co-crystals can be viewed as a special case of solvates and hydrates, wherein the second component, the coformer, is not a solvent (including water), and is typically nonvolatile.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on "Regulatory Classification of Pharmaceutical Co-Crystals." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. This guidance refers to information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR 314.50(d)(1) and 314.94(a)(5) and (a)(9) have been approved under OMB control number 0910-0001.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <https://www.regulations.gov>.

Dated: February 9, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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